Complete Summary

GUIDELINE TITLE

Guidelines for the number of embryos to transfer following in vitro fertilization.

BIBLIOGRAPHIC SOURCE(S)

Min JK, Claman P, Hughes E, Society of Obstetricians and Gynaecologists of Canada, Canadian Fertility and Andrology Society. Guidelines for the number of embryos to transfer following in vitro fertilization. J Obstet Gynaecol Can 2006 Sep;28(9):799-813. [147 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

- Infertility
- In vitro fertilization

GUIDELINE CATEGORY

Counseling
Evaluation
Prevention

CLINICAL SPECIALTY

Endocrinology
Family Practice
Internal Medicine
Obstetrics and Gynecology

INTENDED USERS

Health Plans
Hospitals
Managed Care Organizations
Physicians

GUIDELINE OBJECTIVE(S)

To review the effect of the number of embryos transferred on the outcome of in vitro fertilization (IVF), to provide guidelines on the number of embryos to transfer in IVF-embryo transfer (ET) in order to optimize healthy live births and minimize multiple pregnancies

TARGET POPULATION

Women undergoing in vitro fertilization-embryo transfer (IVF-ET)

INTERVENTIONS AND PRACTICES CONSIDERED

1. Identify specific determinants of implantation in order to minimize the occurrence of multifetal gestation
2. Consider transfer of fewer blastocyst stage embryos than cleavage stage embryos
3. Determine the number of cleavage stage embryos to transfer according to woman's age and viability, but whenever reasonable, consider the transfer of a single embryo
4. Consider age of donor
5. Refer to maternal-medicine specialist, if indicated
6. Counsel couples on risks of multifetal gestation
7. Limit iatrogenic multiple pregnancies from ovarian stimulation

MAJOR OUTCOMES CONSIDERED

- Clinical pregnancy rate
- Multiple pregnancy rate
- Live birth rate

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Patient Registry Data

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The Cochrane Library and MEDLINE were searched for English language articles from 1990 to April 2006. Search terms included embryo transfer (ET), assisted reproduction, in vitro fertilization (IVF), intracytoplasmic sperm injection (ICSI), multiple pregnancy, and multiple gestation. Additional references were identified through hand searches of bibliographies of identified articles.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Quality of Evidence Assessment*

I: Evidence obtained from at least one properly randomized controlled trial

II-1: Evidence from well-designed controlled trials without randomization

II-2: Evidence from well-designed cohort (prospective or retrospective) or case-control studies, preferably from more than one centre or research group

II-3: Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category

III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

*Adapted from the Evaluation of Evidence criteria described in the Canadian Task Force on Periodic Health Exam.

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Classification of Recommendations*

A. There is good evidence to recommend the clinical preventive action.
B. There is fair evidence to recommend the clinical preventive action.
C. The existing evidence is conflicting and does not allow to make a recommendation for or against use of the clinical preventive action; however, other factors may influence decision-making.
D. There is fair evidence to recommend against the clinical preventive action.
E. There is good evidence to recommend against the clinical preventive action.

*Adapted from the Classification of Recommendations criteria described in the Canadian Task Force on the Periodic Health Exam.

COST ANALYSIS

Published cost analyses were reviewed.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

This guideline was reviewed by the Reproductive Endocrinology and Infertility Committee and the Maternal-Fetal Medicine Committee and approved by the Executive and Council of the Society of Obstetricians and Gynaecologists of Canada (SOGC) and the Board of the Canadian Fertility and Andrology Society.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions of the levels of evidence (I, II-1, II-2, II-3, and III) and grades of recommendations (A-E) are provided at the end of the "Major Recommendations" field.

The recommendations made in this guideline were derived mainly from studies of cleavage stage embryos—those cultured for two or three days.

Limiting the Number of Embryos to Transfer in In Vitro Fertilization-Embryo Transfer (IVF-ET)

1. Individual IVF-ET programs should evaluate their own data to identify patient-specific, embryo-specific, and cycle-specific determinants of implantation and live birth, in order to develop embryo transfer policies that minimize the occurrence of multifetal gestation while maintaining acceptable overall pregnancy and live birth rates. (**III-B**)

Cleavage Stage versus Blastocyst Stage Embryos

2. In general, consideration should be given to the transfer of fewer blastocyst stage embryos than cleavage stage embryos, particularly in women with excellent prognoses and high-quality blastocysts. (**I-A**)

Women under Age of 35 Years

Summary Statement

The following recommendations are generally intended for cleavage stage embryos transferred on day two or three. Because blastocyst stage embryos have higher implantation rates than cleavage stage embryos, fewer blastocyst stage embryos may need to be transferred. (**II**)

3. In women under the age of 35 years, no more than two embryos should be transferred in a fresh IVF-ET cycle. (**II-2A**)

Elective Single Embryo Transfer

Estimated Impact of Elective Single Embryo Transfer (eSET)

4. In women under the age of 35 years with excellent prognoses, the transfer of a single embryo should be considered. Women with excellent prognoses include those undergoing their first or second IVF-ET cycle or one immediately following a successful IVF-ET cycle, with at least two high-quality embryos available for transfer. (**I-A**)

Women Aged 35 to 39 Years

5. In women aged 35 to 37 years, no more than three embryos should be transferred in a fresh IVF-ET cycle. In those with high-quality embryos and favourable prognoses, consideration should be given to the transfer of one or two embryos in the first or second cycle. (**II-2A**)
6. In women aged 38 to 39 years, no more than three embryos should be transferred in a fresh IVF-ET cycle. (**III-B**) In those with high-quality embryos and favourable prognoses, consideration should be given to the transfer of two embryos in the first or second cycle. (**III-B**)

Women Aged over 39 Years

7. In women over the age of 39 years, no more than four embryos should be transferred in a fresh IVF-ET cycle. (**III-B**) In those older women with high-quality embryos in excess of the number to be transferred, consideration

should be given to the transfer of three embryos in the first IVF-ET cycle. (**III-B**)

Poor Prognosis

8. In exceptional cases when women with poor prognoses have had multiple failed fresh IVF-ET attempts, consideration may be given to the transfer of more embryos than recommended above in subsequent fresh IVF-ET cycles. (**III-C**)

Donor-Recipient Cycles

9. In donor–recipient cycles, the age of the oocyte/embryo donor should be used when determining the number of embryos to transfer. (**II-2B**)

Medical Single Embryo Transfer

10. In women with obstetrical or medical contraindication to multifetal gestation, fewer embryos should be transferred to minimize the chance of multifetal gestation. In such cases, pre-treatment consultation with a maternal-fetal medicine specialist should be pursued. (**III-C**) Whenever reasonable, consideration should be given to the transfer of a single embryo. (**II-3B**)

Attitudes towards Multifetal Gestation

11. Couples should be adequately counselled regarding the obstetrical, perinatal, and neonatal risks of multifetal gestation to facilitate informed decision making regarding the number of embryos to transfer. (**II-3B**) Emphasis on healthy singleton live birth as the measure of success in IVF-ET may be beneficial in promoting a reduction in the number of embryos transferred. (**III-C**)

Economic Considerations

12. A strategy for public funding of IVF-ET must be developed for the effective implementation of guidelines limiting the number of embryos transferred. In the context of this strategy, total health care costs would be lower as a result of reductions in the incidence of multifetal pregnancies and births. (**III-C**)

Non-IVF-ET Infertility Treatments and Multifetal Gestation

13. Efforts should be made to limit iatrogenic multiple pregnancies resulting from non–IVF-ET ovarian stimulation, through the development of suitable guidelines for cycle cancellation and the removal of financial barriers to IVF-ET. (**III-B**)

<u>Definitions</u>:

Quality of Evidence Assessment*

I: Evidence obtained from at least one properly randomized controlled trial

II-1: Evidence from well-designed controlled trials without randomization

II-2: Evidence from well-designed cohort (prospective or retrospective) or case-control studies, preferably from more than one centre or research group

II-3: Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category

III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

Classification of Recommendations**

A. There is good evidence to recommend the clinical preventive action.
B. There is fair evidence to recommend the clinical preventive action.
C. The existing evidence is conflicting and does not allow to make a recommendation for or against use of the clinical preventive action; however, other factors may influence decision-making.
D. There is fair evidence to recommend against the clinical preventive action.
E. There is good evidence to recommend against the clinical preventive action.

*The quality of evidence reported in these guidelines has been adapted from the Evaluation of Evidence criteria described in the Canadian Task Force on the Periodic Health Exam.

**Recommendations included in these guidelines have been adapted from the Classification of Recommendations criteria described in the Canadian Task Force on the Periodic Health Exam.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

This guideline is intended to minimize the occurrence of multifetal gestation, particularly high-order multiples (HOM), while maintaining acceptable overall pregnancy and live birth rates following in vitro fertilization-embryo transfer (IVF-ET).

POTENTIAL HARMS

Not stated

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- Given the rapidity of advances in in vitro fertilization-embryo transfer (IVF-ET), it must be acknowledged that these recommendations will require regular revision to accurately reflect ongoing improvements in implantation rates.
- This guideline reflects emerging clinical and scientific advances as of the date issued and is subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed. Local institutions can dictate amendments to these opinions. They should be well documented if modified at the local level.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Min JK, Claman P, Hughes E, Society of Obstetricians and Gynaecologists of Canada, Canadian Fertility and Andrology Society. Guidelines for the number of embryos to transfer following in vitro fertilization. J Obstet Gynaecol Can 2006 Sep;28(9):799-813. [147 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2006 Sep

GUIDELINE DEVELOPER(S)

Society of Obstetricians and Gynaecologists of Canada - Medical Specialty Society

SOURCE(S) OF FUNDING

Society of Obstetricians and Gynaecologists of Canada

GUIDELINE COMMITTEE

Reproductive Endocrinology and Infertility Committee
Maternal Fetal Medicine Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Society of Obstetricians and Gynaecologists of Canada Web site.

Print copies: Available from the Society of Obstetricians and Gynaecologists of Canada, La société des obstétriciens et gynécologues du Canada (SOGC) 780 promenade Echo Drive Ottawa, ON K1S 5R7 (Canada); Phone: 1-800-561-2416

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI Institute on February 11, 2009. The information was verified by the guideline developer on March 10, 2009.

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Date Modified: 4/6/2009